SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Coronary Stent System

Device Trade Name: Driver™ Over-The-Wire, Rapid Exchange and Multi-Exchange Coronary Stent System

Applicant's Name and Address:
Medtronic Vascular
3576 Unocal Place
Santa Rosa, CA 95403
USA

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P030009

Date of Notice of Approval to Applicant: October 1, 2003

II. INDICATIONS FOR USE

The Medtronic Driver™ Over-The-Wire, Rapid Exchange, and Multi-Exchange Coronary Stent Systems (hereinafter called the Driver™ Coronary Stent System) are indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete *de novo* or restenotic lesions with reference vessel diameters of 3.0 – 4.0 mm and ≤ 30 mm in length using direct stenting or pre-dilatation. Outcome beyond 270 days for this permanent implant is unknown at present.

III. DEVICE DESCRIPTION

The Medtronic Driver™ Coronary Stent System is comprised of two components: the Stent and the Delivery System. The Driver™ stent is identical despite which delivery system it is mounted on.

The Driver™ stent consists of a series of 1.0 mm segments that are constructed from a continuous toroid ring manufactured from a Co-Ni-Cr-Mo alloy conforming to ASTM F 562-00. The ring is formed into alternating upper and lower crowns with 10 radiused crowns per end connected by axial struts for a total of 20 crowns and 20 axial struts in a zigzag pattern.

The use of a new alloy facilitates the implementation of thinner struts without affecting the radial strength or radiopacity of the stent. Unlike 316L stainless steel, the new alloy does not contain significant levels of iron (1.0 percent by weight maximum), thereby enhancing MRI compatibility. In addition, the radiopacity of the Co-Ni-Cr-Mo alloy is greater than that of 316L stainless steel, due primarily to increased levels of molybdenum. As such, the radiopacity of 316L stainless steel stents is maintained with the Co-Ni-Cr-Mo alloy stents even with thinner stent struts

The stent is mounted on one of three delivery systems. Each delivery system provides a means for delivering the stent through the coronary vasculature and, once in the desired location, expands the stent through balloon inflation. The three delivery systems available with the Driver™ stent are the Over-The-Wire (OTW), Rapid Exchange (RX) and Multi Exchange (MX) Delivery System.

All delivery systems have a minimal amount of working length extending beyond the stent on each side. The inner lumen of the catheter is designed to accommodate a maximum guidewire diameter of 0.014 inches.

Table 1 provides the product labeling specifications for the Medtronic Driver™ Coronary Stent and the three Delivery Systems

Table 1: Product Labeling Specifications for the Medtronic Driver™ Coronary Stent Systems

Product	Delivery System Type	Stent Diameter (mm)	Stent Length (mm)	Minimum Guiding Catheter Inner Diameter (inches)	Nominal Pressure (atm)	Rated Burst Pressure (atm)
Medtronic Driver™ Over-the-Wire Coronary Stent System	Over-the-Wire	3.0 3.5 4.0	9 12 15 18 24 30	.056	9	16
Medtronic Driver™ Rapid Exchange Coronary Stent System	Rapid Exchange	3.0 3.5 4.0	9 12 15 18 24 30	.056	9	16
Medtronic Driver™ Multi-Exchange MX Coronary Stent System	Multi-Exchange	3.0 3.5 4.0	9 12 15 18 24 30	.064	9	16

IV. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

Contraindications

The Driver Coronary Stent System is contraindicated for use in:

- Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon.

Warnings and Precautions

A list of warnings and precautions can be found in the device labeling.

V. ALTERNATIVE PRACTICES AND PROCEDURES

Patients with early coronary artery disease receive exercise, diet, and drug therapy as appropriate. If the disease progresses, alternative practices specific to the treatment of coronary artery disease include: percutaneous transluminal coronary angioplasty (PTCA), drug therapy (e.g., thrombolytic agents, antiplatelet agents, and anticoagulant agents), Coronary Artery Bypass Graft Surgery (CABG), and stenting with other commercially available stents.

VI. MARKETING HISTORY

The Driver Coronary Stent System has been approved for commercial distribution in the European Union, Canada, China, Australia and Singapore. The Driver Coronary Stent System has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VII. SUMMARY OF PRECLINICAL STUDIES

Biocompatibility

All biocompatibility testing was performed in accordance with;

- Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices; published by the Interventional Cardiology Devices Branch, Division of Cardiovascular, Respiratory and Neurology Devices, Office of Device Evaluation in May 1995.
- ISO 10993, Biological Evaluation of Medical Devices

The following biocompatibility tests were conducted and passed on the Driver™ Coronary Stent System:

Biocompatibility Testing on Co-Ni-Cr-Mo alloy (Driver™ Stent)

Component	Biological Effect	Test	Criterion	Results
Stent Raw Material	Cytotoxicity	L929 MEM Elution Test-ISO	01-2293-G1 Results must indicate a grade of 2 or lower.	Pass
	Sensitization	Skin Sensitization Kligman Maximization test-ISO	01-2293-G11 No dermal inflammatory response greater than the control.	Pass
	Irritation	Intracutaneous Injection Test-ISO	01-2293-G8 No greater adverse reactions or responses when compared to the controls.	Pass
	Systemic Toxicity	System Injection test-ISO	01-2293-G9 No greater adverse reactions or responses when compared to the controls.	Pass
	Mutagenicity / Genotoxicity	Rodent Bone Marrow Micronucleus Assay-ISO	01-2293-G7 The test article must not induce a significant increase in the number of micronucleated cells when compared to controls.	Pass
		Chromosomal Aberration Assay-ISO	01-2293-G6 The test article must not induce a significant increase in reversion in the genomes of the organisms tested, when compared to controls.	Pass
		S. typhimurium/ E.coli Reverse Mutation Assay-ISO	01-2293-G5 Test article extracts must not be considered mutagenic when compared to controls.	Pass
	Implantation / Subchronic toxicity	Biocompatibility Implant Study	0052D640 P1056 No capsule formation or other adverse reaction to the implanted test article.	Pass
	Hemocompatibility	C3a Complement Activation Assay	01-2293-G3 The test article must not induce complement activation when compared to controls.	Pass

		Unactivated Partial Thromboplastin Time Assay-ISO	01-2293-G4 The test article must not significantly effect the clotting time of human plasma when compared to controls.	Pass
		In Vitro Hemocompatibility Assay-ISO	01-2293-G2 The test article must not adversely effect selected hematological parameters of human blood when compared to controls.	Pass
	Pyrogenicity	Rabbit Pyrogen Test (Material Mediated)-ISO	01-2293-G10 No single animal must exhibit an increase of 0.5°C or more above its baseline temperature.	Pass
	Hemocompatibility	C3a Complement Activation Assay	01T 10878 01 The test article must not induce complement activation when compared to controls.	Pass
	Implantation / Subchronic toxicity	ISO Muscle Implantation, in 3 Rabbits (6 weeks), w/histopathology	01C 12404 00 No capsule formation or other adverse reaction to the implanted test article.	Pass

Biocompatibility Testing on Stent and Rapid Exchange Delivery System

Component	Type	Test	Criterion	Results
Stent and Delivery System	Cytotoxicity	L929 MEM Elution Test-ISO	01C 11441 00 Results must indicate a grade of 2 or lower.	Pass
	Sensitization	ISO Sensitization Study in the Guinea Pig	01C 11441 00 No dermal inflammatory response at the test sites greater than that seen in the control.	Pass
	Irritation	ISO Acute Intracutaneous Reactivity Study in the Rabbit	01C 11441 00 No adverse reactions or responses when compared to the controls.	Pass
	Systemic Toxicity	ISO Acute Systemic Toxicity in the Mouse	01C 11441 00 No greater adverse reactions or responses when compared to the controls.	Pass

	Mutagenicity / Genotoxicity	Genotoxicity: Bacterial Reverse Mutation (Ames) Test, Salmonella and *E.coli* Strains	01C 12359 00 The test article must not induce a significant increase in reversion in the genomes of the organisms tested, when compared to controls. Test article extracts must not be considered mutagenic when compared to controls.	Pass
	Hemocompatibility	Hemolysis	01C 11441 00 The mean hemolytic index must be 2% or less.	Pass
		White Blood Cell Morphology Study –*In vitro*	01T 10878 00 The number of while cells with morphological abnormalities must be <5%.	Pass
	Hemocompatibility	Plasma Recalcification Time Coagulation Study (With Protocol Amendment *I, II & III)* V0020-000	01T 10878 00 The test article must not exhibit a significant difference in recalcification times and effects on fibrin clot formations when compared to the control.	Pass
	Pyrogenicity	ISO Rabbit Pyrogen Study (Material Mediated)	01C 11441 00 No single animal must exhibit an increase of 0.5°C or more above its baseline temperature.	Pass

Biocompatibility Testing on the Multi-Exchange Delivery System

Component	Type	Test	Criterion	Results
Delivery System	Cytotoxicity	L929 MEM Elution Test-ISO	02T0757800 Results must indicate a grade of 2 or lower.	Pass
	Hemocompatibility	Hemolysis	02T0757800 The mean hemolytic index must be 2% or less.	Pass
		C3a Complement Activation	02T0626800 The test article must not induce complement activation when compared to controls.	Pass
		Plasma Recalcification	02T0626800 The test article must not exhibit a significant difference in recalcification times when compared to the control.	Pass
		Thromboresistance	02T0692000 Test articles are evaluated for the presence of thrombus as compared to the controls.	Pass

	Irritation	ISO Acute Intracutaneous Reactivity	02T0626800 02T0692000 No greater adverse reactions or responses when compared to the controls.	Pass Pass
	Systemic Toxicity	ISO Acute System Toxicity	02T0626800 02T0692000 No greater adverse reactions or responses when compared to the controls.	Pass Pass
	Genotoxicity	Ames	02T0626800 02T0692000 Test article extracts must not be considered mutagenic.	Pass Pass
	Physicochemical	Physicochemical (aq) Physicochemical (Non-aq)	02T0757800 Non-volatile residue: < 15mg Residue on Ignition: <5mg Heavy Metals: ≤ 1ppm Buffering Capacity: <10ml 02T0757800 No acceptance criteria have been determined. For characterization only.	Pass Pass
	Sensitization	ISO Sensitization	02T0332300 02T0692000 96T0594800 97C0609000 00C1014200 No dermal inflammatory response at the test sites greater than that seen in the control.	Pass Pass Pass Pass Pass

The Medtronic Driver™ Stent Delivery System successfully passed all the above referenced biocompatibility testing. The Driver™ Over-The-Wire Delivery System was not tested since the materials found in it are identical to the materials found in the two systems (Rapid Exchange and Multi-Exchange) which passed all tests noted above.

Sterilization

The Driver™ Stent System will be sterilized using Electron Beam sterilization and has been validated per AAMI/ISO 11137: Sterilization of health care products - Requirements for validation and routine control - Radiation sterilization.

Results obtained from the sterilization studies show that the device satisfies a minimum Sterility Assurance Level (S.A.L.) of 10^{-6}.

***In Vitro* Testing**

In vitro bench testing of the Medtronic Driver™ Stent Delivery Systems was conducted in accordance with the FDA ODE "Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices: PTCA Catheters,

Atherectomy Catheters, Lasers, Intravascular Stents", May 1995. The relevant tests outlined in the guidance were conducted to demonstrate the functional performance characteristics of the device.

The following is a brief summary of the bench testing conducted on the device:

Material Analysis (stent)
This study was conducted to verify that Driver™ stents are produced from material that conforms to the chemical composition requirements of ASTM F562-00, "Standard Specification for Wrought Cobalt-35 Nickel-20 Chromium-10 Molybdenum Alloy for Surgical Implant Applications". Data for this test was collected from Co-Ni-Cr-Mo alloy tubes as processing of this material into a completed stent does not change the overall composition of the material. The material used to manufacture the Driver™ stent conformed to ASTM F562-00.

Scanning Electron Microscopy (SEM)
SEM analysis was conducted at 200x magnification to identify trace contaminants that may be present on the Driver™ stent surface. No foreign material was observed on any of the production lot stents tested. Several small particles inherent to the base stent material were observed on the surface, which most probably were exposed during stent electropolishing during the manufacturing procedure.

Mechanical Properties
This testing was conducted to characterize the following mechanical properties of annealed Co-Ni-Cr-Mo alloy: 0.2% offset yield strength, ultimate tensile strength, percent elongation, and reduction of area. Five (5) tensile bars were machined from barstock conforming to ASTM F562-00. The bars were then vacuum annealed to product an ASTM grain size of 8.5 in the gage sections. The bars were tensile tested to failure while engineering stress and strain were continuously recorded. The offset yield strength, ultimate tensile strength, percent elongation, and percent reduction of area for the Driver™ stent material are in conformance with ASTM F562-00.

Corrosion
This test was conducted to evaluate the relative susceptibility to localized corrosion of finished Driver stent components. The analysis was based upon ASTM G61, "Standard Test Method for Conducting Cyclic Potentiodynamic Polarization Measurements for Localized Corrosion Susceptibility of Iron, Nickel, or Cobalt-Based Alloys". The results indicated that the Driver™ stent possesses a high resistance to the onset of localized corrosion.

Stent Free-area
The Percent Free-Area is a value calculated using Driver stent nominal dimensional values and is based in the ratio of stent area to the area of the vessel. Metal to artery percentage ratios ranged from 15.4% to 20.5% for 3.0mm to 4.0mm stent, respectively.

Length Change vs. Diameter
This test was performed to determine the change in length as a function of stent internal diameter. The testing was performed on complete stent delivery systems that had been subjected to all manufacturing and sterilization procedures. Each stent was measured for initial length while still on the delivery system, then deployed to nominal pressure of 9 ATM and measured after removal from the delivery system. Length change ranged from –3% to +4% and met the acceptance criteria.

Stent Uniformity
This test was conducted to demonstrate that the deployed internal diameter of the Driver stent is consistent with labeling. The testing was performed on complete stent delivery systems that had been subjected to all manufacturing and sterilization procedures. Each stent was deployed to nominal pressure of 9ATM. The stent inner diameter was measured at each end. All Driver stents met the uniformity expansion specification of +/- 10% from nominal labeled diameter to 9ATM. The results indicated that the Driver stent expands uniformly at all diameters and maintains this uniformity upon withdrawal of the balloon.

Radial Strength
This test is conducted to determine and graphically represent the change in stent internal diameter as a function of circumferential pressure and to determine the pressure at which deformation is no longer completely reversible for the Driver stent. Fifteen (15) 3.0mm and fifteen (15) 4.0mm stents were subjected to all stent-manufacturing procedures. The stents were deployed to nominal pressure and removed from the delivery system. The stents were placed into a sleeve approximately 1mm larger then the stent diameter. A vacuum was then applied and outer diameter measurements taken at various pressures. All samples maintained a minimum of at least 50 percent of the original stent diameter after a 254mm Hg pressure was radially applied. All samples met the acceptance criteria.

Bent Radial Fatigue Testing
This test was conducted to determine the radial fatigue integrity on a bend of a Driver stent under accelerated cycling designed to test expected *in vivo* conditions. Eighty-two (82) Driver stents were deployed up to a maximum of 5.1mm in distendable tubing and attached to fatigue equipment that underwent a 0.005" distention. There were no stent failures noted after 420 million cycles which is equivalent to 10 years *in vivo*.

Stent Recoil
This test was conducted to quantify the amount of elastic recoil. Fifteen (15) stent delivery systems of each length and diameter (excluding 3012 and 4012) were subjected to all manufacturing and sterilization procedures. The stent delivery system was inflated to nominal pressure (9ATM) and the stent was removed allowing for recoil to occur. The inner diameter at each end of the stent was recorded. Recoil was calculated subtracting the recoiled stent inner diameter from the pre-recoil inner diameter. Average recoil ranged from 0.002 to 0.004 inches. All stents met the acceptance criteria after balloon inflation to nominal pressure.

MRI

Driver Stents were tested to ensure they did not react to a magnetic field in such a manner that might pose a clinical issue. The stents should neither deflect nor produce appreciable susceptibility image artifacts in the presence of a magnetic field.

Testing for image artifacts created by the Driver stents in a 1.5 Tesla magnetic field produced minimal artifact susceptibility. This result was expected in the light of the lack of iron in the material composition. The mean deflection angle measured for the Driver stent in association with testing performed using a 3.0 Tesla field was 3°.

In conclusion, the Driver stents tested did not cause distortion of the magnetic field during the MRI procedure. If an implant deflects less than 45°, then the magnetically induced deflection force is less than the force on the implant due to gravity. Accordingly, since the stents tested had a mean deflection of 3°, a negligible risk of stent movement in a 3.0 Tesla MRI field was indicated.

Stent Expansion

This test is conducted to determine if the plastic deformation experienced by the stent when expanded from the compressed profile to the final maximum deployed diameter can produce crack initiation for the Driver stent. Fifteen (15) samples from each length and diameter (excluding the 3012 and 4012) were deployed to their largest possible diameters by inflating each delivery system to balloon failure. Each stent was examined at 45X magnification for potential cracks. All samples met the acceptance criteria with no visible cracks or notches.

Dimensional Verification (stent)

This test is conducted to verify that dimensional and visual specifications for the Driver stent can be achieved. Fifteen (15) samples from each length within 3.0 and 3.5mm diameters were measured with a toolmaker's microscope. All samples met the dimensional specifications.

Maximum Pressure (burst test)

This test is conducted to demonstrate that the delivery system (with mounted stent) will not experience balloon, shaft, proximal adaptation or proximal/distal seal loss of integrity at or below the pressure required to expand the stent to its labeled diameter. Stent delivery systems that had been subjected to all manufacturing and sterilization procedures were pressurized to 90psi with pressure held for 15 seconds and released for 3 seconds. The cycle was then repeated, increasing inflation pressure by 15psi each cycle until failure. The shaft of all delivery systems remained intact throughout the test and resulted in a labeled rated burst pressure of 16 ATM.

Stent Diameter vs. Pressure (stent compliance)

This test is conducted to quantify the stent inner diameter as a function of balloon inflation pressure. Each delivery system was inflated to 6ATM and the outer diameter at the distal and proximal point of the stent was measured. This was repeated at 1ATM increments. Once the OD measurement was taken at 9ATM, the system was deflated, the

stent was removed and the inner diameter was measured. The stent was placed back on the balloon and continued 1ATM increments until balloon failure. All stent delivery system met the acceptance criteria requirements.

Bond Strength
This test was performed to provide data to support the bond strength specifications for the Driver Stent Delivery Systems. All bonds were trimmed to manageable lengths and loaded into the tensile tester and pulled to failure. All samples met the acceptance criteria.

Diameter and Profile
This test was conducted to provide dimensional data for the tip, balloon bond, distal shaft, intermediate shaft, and proximal shaft of the Driver Coronary Stent System. All catheter diameters and profiles met all acceptance criteria.

Balloon Deflatibility
This test is conducted to provide assurance that the deflated delivery system balloons will not interfere with the Driver deployed stent *in vivo*. Complete stent delivery systems were inflated to nominal pressure (9ATM) with a replica vessel placed over the premounted stent. The stent delivery system was then deflated and vacuum was drawn, allowing the stent to release from the delivery system. All samples passed the acceptance requirement of either gravity or vessel release.

Balloon Deflation Time
This test is conducted to quantify the deflation time of the Driver stent delivery system. The complete stent delivery systems were inflated to 9 ATM. Simultaneously, a vacuum was pulled and a timer started. The amount of time to deflate the balloon from nominal pressures was recorded. The results indicated that all Driver Coronary Stent Systems could be deflated within a clinically acceptable time.

Balloon Fatigue
This report summarizes the testing done to satisfy all regulatory requirements for balloon fatigue on the Driver Coronary Stent System. The stent delivery systems were repeatedly inflated to demonstrate the balloon could sustain multiple repeated inflations. The stent delivery systems were capable of at least 20 inflations to rated burst pressure.

Crossing Profile
This test is conducted to verify the crossing profile as per label claims and to discuss the clinical relevance of this test. The stent delivery systems are inserted through a crossing profile block until the smallest block that the stent could pass through was determined. All samples passed through the 0.056" hole gauge with a maximum observed crossing profile of 0.049".

Tortuous Path
Stent retention is evaluated using a test which involves tracking the device back and forth five times through a track fixture that has four bends of varying tortuosity. After tracking,

the force required to remove the stent from the delivery system is measured and the initial peak force observed during testing is recorded. Devices are required to meet a pre-determined retention force with a 95% confidence and 95% reliability.

***In vivo* (animal) studies**

Medtronic has conducted six GLP animal studies utilizing the Driver Coronary Stent Systems in accordance with 21 CFR § 58. These studies evaluated safety, efficacy and overall device performance; summaries of these studies are included in the following table:

Summary of GLP Studies Performed

Study #	Stent Design (Delivery System)	# of Animals	# of Stents	Follow-up Duration	Endpoints
FS62	3.0–4.5mm* dia. x 18mm lngth. (OTW and RX Delivery Systems) Control = S7	8	19	28-days	Acute delivery, mechanical performance, and chronic vascular response.
FS65	3.0–3.5mm dia. x 18mm lngth. (OTW Delivery System) Control = S7	6	16	28-days	Acute delivery and deployment performance, angiographic estimates of in-stent restenosis at sacrifice and histomorphometric analysis of histology.
FS66	3.0–3.5mm dia. x 18mm lngth. (OTW Delivery System) Control = S7	4	10	90-days	Acute delivery and deployment performance, angiographic estimates of in-stent restenosis at sacrifice and histomorphometric analysis of histology.
FS67	3.0–3.5mm dia. x 18mm lngth. (OTW Delivery System) Control = S7	6	16	180-days	Acute delivery and deployment performance, angiographic estimates of in-stent restenosis at sacrifice and histomorphometric analysis of histology.
FS81	3.0–3.5mm dia. x 18mm lngth. (OTW Delivery System) Control = S7	6	9	180-days	Acute delivery and deployment performance, angiographic estimates of in-stent restenosis at sacrifice and histomorphometric analysis of histology.
FS87	3.5mm dia. x 18mm lngth. (OTW and RX Delivery Systems) . Control = S7	1	8	Acute	Acute delivery and mechanical performance of Over-the-Wire and Rapid Exchange stent systems.

* The 4.5mm Driver stent was included in this pre-clinical study but is not part of this PMA Application

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The Medtronic Driver DeNovo and Restenotic Registry enrolled 298 patients in a non-randomized, multi-center study. These patients form the basis of the observed events reported in the following section.

Driver DeNovo and Restenotic Registry

A total of 298 patients were enrolled in a multi-center registry to evaluate the safety and efficacy of the Medtronic Driver Coronary Stent System for treatment of symptomatic coronary artery disease.

The primary endpoint of MACE at 180 days was compared to an objective performance criterion (OPC) of 15% based on a pooled MACE rate derived by pooling the data from the Bard XT Stent EXTRA RCT, Medtronic Micro Stent II SMART RCT, and Medtronic BeStent I (BEST) & BeStent II Registries.

Adverse events reported during the first six and nine months are shown in the table below. A total of 25 of 298 patients (8.4%) who received the Medtronic Driver stent experienced one or more adverse events during the nine months of follow-up.

A total of 4 of the 298 (1.3%) patients who received the Driver stent died during the clinical study. These out-of-hospital deaths were all non-cardiac related: one secondary to ovarian cancer at 43 days post-procedure, one secondary to a brain tumor at 136 days post-procedure, one due to acute respiratory failure at 242 days post-procedure and one non-specified cancer death at 268 days post-procedure. There were no instances of stent thrombosis during the first 270 days. The incidence of vascular complications was 3.4% (10/298). The rate of bleeding complications was 2.3% (7/298).

There were no (0/298) delivery or device failures reported.

Principal Adverse Events Through 180 & 270 Days

Driver DeNovo and Restenotic Registry

%, (Number) [95% confidence interval]

Complication*	Medtronic Driver Stent (N=298) 180-Day Results	Medtronic Driver Stent (N=298) 270-Day Results
Adverse Event§	**7.7%** (23)[5.0%,11.4%]	**8.4%** (25)[5.5%,12.1%]
In-Hospital	**5.7%** (17)[3.4%,9.0%]	**5.7%** (17)[3.4%,9.0%]
Out-of-Hospital	**2.0%** (6)[0.7%,4.3%]	**2.7%** (8){1.2%,5.2%]
MACE	**5.7%** (17)[3.4%,9.0%]	**10.1%** (30) [6.9%,14.1%]
In-Hospital	**1.7%** (5)[0.5%,3.9%]	**1.7%** (5)[0.5%,3.9%]
Out-of-Hospital	**4.0%** (12)[2.1%,6.9%]	**8.4%** (25) [5.5%,12.1%]
Death	**0.7%** (2)[0.1%,2.4%]	**1.3%** (4) [0.4%, 3.4%]**
In-Hospital	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]

Out-of-Hospital	**0.7%** (2)[0.1%,2.4%]	**1.3%** (4) [0.4%,3.4%]**
Q-wave MI	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
In-Hospital	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
Out-of-Hospital	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
Non Q-wave MI	**1.7%** (5)[0.5%,3.9%]	**1.7%** (5)[0.5%,3.9%]
In-Hospital	**1.7%** (5)[0.5%,3.9%]	**1.7%** (5)[0.5%,3.9%]
Out-of-Hospital	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
Target Lesion Revascularization	**3.4%** (10) [1.6%,6.1%]	**7.0%** (21) [4.4%, 10.6%}
In Hospital -PTCA	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
In Hospital-CABG	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
Out-of-Hospital PTCA	**2.7%** (8)[1.2%,5.2%]	**6.4%** (19) [3.9%, 9.8%]
Out-of-Hospital CABG	**0.7%** (2) [0.1%,2.4%]	**0.7%** (2) [0.1%,2.4%]
Emergent CABG	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
In-Hospital	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
Out-of-Hospital	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
Stent Thrombosis	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
In-Hospital	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
Out-of-Hospital	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
Bleeding (procedural transfusion)	**2.3%** (7)[0.9%,4.8%]	**2.3%** (7)[0.9%,4.8%]
In-Hospital	**2.0%** (6)[0.7%,4.3%]	**2.0%** (6)[0.7%,4.3%]
Out-of-Hospital	**0.3%** (1)[0.0%,1.9%]	**0.3%** (1)[0.0%,1.9%]
CVA	**0.3%** (1)[0.0%,1.9%]	**0.3%** (1)[0.0%,1.9%]
In-Hospital	**0.0%** (0)[0.0%,1.2%]	**0.0%** (0)[0.0%,1.2%]
Out-of-Hospital	**0.3%** (1)[0.0%,1.9%]	**0.3%** (1)[0.0%,1.9%]
Vascular Complications	**3.4%** (10)[1.6%,6.1%]	**3.4%** (10)[1.6%,6.1%]
In-Hospital	**2.7%** (8)[1.2%,5.2%]	**2.7%** (8)[1.2%,5.2%]
Out-of-Hospital	**0.7%** (2)[0.1%,2.4%]	**0.7%** (2)[0.1%,2.4%]
Stent Delivery Failures	**0.0%** (0) [0.0%, 1.2%]	**0.0%** (0) [0.0%, 1.2%]

*Complications are based on patient totals. Seven patients had multiple adverse events: one patient had 3 vascular complications, four patients had 2 vascular complications), one patient had 1 non-Q MI and 1 bleeding. complication), and one patient had1 non-Q MI and 1 vascular complication.

§Adverse Event= Death, Q or Non-Q wave MI, Emergent CABG, Stent Thrombosis, CVA, Bleeding Complications, and Vascular Complications.
**All four deaths were non-cardiac.
Definitions for the terms used in Table 2 are found in the footnotes to Table 3.

Potential adverse events that may be associated with the use of a coronary stent in native coronary arteries (including those listed in Table 2) are listed below in order of severity:

- Death
- Emergency Coronary Artery Bypass Graft Surgery (CABG)
- Stroke/Cerebrovascular Accidents
- Cardiac tamponade
- Stent thrombosis or occlusion
- Total occlusion of coronary artery
- Acute myocardial infarction

- Restenosis of stented segments
- Perforation
- Arrhythmias, including ventricular fibrillation & ventricular tachycardia
- Dissection
- Emboli, distal (air, tissue or thrombotic emboli)
- Stent embolization
- Hemorrhage requiring transfusion
- Pseudoaneurysm, femoral
- Spasm
- Myocardial ischemia
- Hypotension/Hypertension
- Allergic reaction to drugs/contrast medium/stent material
- Peripheral ischemia
- Peripheral nerve injury
- Infection and pain at the insertion site
- Hematoma

IX. SUMMARY OF CLINICAL STUDIES

Purpose

The purpose of the Driver Registry was to evaluate the safety and efficacy of the Medtronic Driver stent for the treatment of single de novo or restenotic post-PTCA (non-stented) lesions in native coronary arteries.

Conclusions

The Driver Registry demonstrated the 180-day and 270-day safety and efficacy of the Driver stent for treatment of patients with *de novo* or restenotic lesions in native coronary arteries.

Design

A prospective, multi-center non-randomized study was conducted in 23 North American clinical sites enrolling 298 patients. Patients were 18 years of age or older with clinical evidence of ischemic heart disease or a positive functional study undergoing elective treatment for a single *de novo* or restenotic (post PTCA, non-stented) lesion in a native coronary artery. Eligible patients had visually estimated stenosis $\geq 50\%$ and $< 100\%$ in a lesion ≤ 30 mm in length located in a major coronary artery or major side branch ≥ 3.0 mm and ≤ 4.0 mm in diameter.

The primary endpoint in the Driver De Novo and Restenotic Registry was Major Adverse Cardiac Event (MACE) rate defined as the composite of death, Q wave and non-Q wave myocardial infarction, emergent bypass surgery, or target lesion revascularization (TLR) at 180 days. The primary endpoint was analyzed on an intent-to-treat basis, defined as patients who had the study device introduced into the guide catheter after determination

that the subject and the target lesion met all inclusion criteria and none of the exclusion criteria.

The primary endpoint of MACE at 180 days was compared to an objective performance criterion (OPC) of 15% plus delta of 6%, based on a pooled MACE rate derived from the Bard XT Stent EXTRA RCT, Medtronic Micro Stent II SMART RCT, and Medtronic BeStent I (BEST) & BeStent II Registries. These studies had a range of 12.1% to 15.7% for MACE at 6 months compared to the Driver Registry 6 month MACE rate of 5.7% (17/298).

Secondary endpoints, (including acute success, target vessel failure (TVF) in hospital, at 14, 30, 180 and 270 days, clinically driven target lesion revascularization (TLR) at 180 and 270 days, binary angiographic restenosis (≥ 50% in-stent diameter stenosis) at 180 days in the 101 patient subset, late loss at 180 days and ischemic, bleeding and vascular complications) were analyzed on a per-protocol evaluable basis, defined as patients who had successful procedures and were available for follow-up.

All patients received the hospital's standard anti-coagulation/anti-platelet regimen for coronary stent implantation. The ACT was kept at therapeutic levels for Percutaneous Coronary Intervention per the hospital standard.

Demographics

Of the 298 patients enrolled, baseline demographics and clinical characteristics showed a mean age of 62.6 years (range 26 to 88 years), 68.1% (203/298) were men, 27.6% (82/297) had a history of diabetes mellitus, 75.9% (221/291) had hyperlipidemia requiring treatment, 28.8% (83/288) were current smokers and 68.4% (201/294) had hypertension requiring treatment.

Methods

Patients in the Driver DeNovo and Restenotic Registry underwent balloon angioplasty (1:1 balloon to artery ratio) after which a stent of the appropriate length and diameter was selected and deployed. The Medtronic Driver Coronary Stent System could be repressurized up to 16 atm to further dilate the stent to assure complete apposition of the stent to the artery wall. If needed, further inflations were performed with a non-compliant balloon with a balloon-to-artery ratio of 1:1.

The anticoagulation regimen administered to 100% of the patients included 325 mg/day of aspirin for at least 14 days; plus either ticlopidine, 250 mg b.i.d. or clopidogrel 75 mg q.d for 14 days. Glycoprotein IIbIIIa platelet inhibitors were administered to 32.6% (97/298) of the patients during the index procedure.

Clinical or telephone follow-up was conducted in-hospital, and at 14, 30, 180 and 270 days post-procedure. A subset of 27.8% (83/298) patients underwent follow-up angiography at the 180 day clinical follow-up. Data monitoring was conducted by

Medtronic personnel. Angiographic films were analyzed and revascularizations were adjudicated by an independent Angiographic Core Laboratory. An independent Clinical Events Committee adjudicated all other primary endpoints and Major Adverse Cardiac Events.

Results

The Driver Registry 180 day TVF rate was 5.0% (15/298) and the TVF rate at 270 days was 9.7% (29/298). Adverse events for both time points are listed in the table found in that section and the Principal Safety and Effectiveness results are presented in the table below.

The primary endpoint of MACE at 180 days was compared to an objective performance criterion (OPC), based on a pooled MACE rate derived from previous AVE/Medtronic/USCI-Bard trials, of 15% plus delta of 6%. Specifically, the OPC of 15% as derived by pooling the data from the Bard XT Stent EXTRA RCT, Medtronic Micro Stent II SMART RCT, and Medtronic BeStent I (BEST) & BeStent II Registries.

A test of the null hypothesis that the observed Driver MACE rate of 5.7% (17/298) is greater or equal to 21% (15% OPC + delta of 6%), provided an Exact Test (one-sided) p-value less than 0.0001, leading to a rejection of this null hypothesis and signifying equivalency with the OPC rate (i.e., Driver MACE rate significantly less than 21%). In a test for superiority, the Driver MACE rate was significantly less than the OPC of 15% itself (p=0.0082).

Gender Bias

No gender bias was noted in The Driver™ Registry. Of the total patients enrolled, 68.1% (203/298) were male. This compares quite closely with the percentage of male patients enrolled in a competitive trial, (GDT Vision, where 68.2% (182/267) of the patient population were male. These percentages reflect the percentage of males in the US cardiac population as a whole.

Principal Effectiveness and Safety Results - Medtronic Driver™ Stent

Efficacy Measures	**Medtronic Driver™ Stent (N=298)**
Post-Procedure In-Stent Minimal Lumen Diameter (mm) Mean±SD (N) Range (min,max)	 2.90±0.42 (284) (1.52,4.12)[2.85 , 2.94]
Procedure In-Stent Percent Diameter Stenosis (% DS) Mean±SD (N) Range (min,max)	 3.05±10.50 (284) (-32.31,41.12)[1.83 , 4.27]
Binary Restenosis Rate	15.7% (13/83)
TLR-free at 180 Days*	96.2% [94.7%, 97.7%]
TLR-free at 270 Days*	91.2% [86.5%, 95.8%]
TVR-free at 180 Days*	95.5% [93.5%, 96.9%]
TVR-free at 270 Days*	90.0% [85.1%, 95.0%]
TVF-free at 180 Days*	92.8% [90.8%, 94.8%]
TVF-free at 270 Days*	88.3% [83.1%, 93.6%]
Safety Measures & Other Clinical Events	**Medtronic Driver™ Stent (N=298)**
Device Success	100.0% (298)[98.8%, 100%]
Procedure Success	98.3% (293)[96.1%, 99.5%]
In-Hospital MACE (Death, QMI,NQMI, TLR, Emergent CABG)	1.7% (5)[0.5%, 3.9%]
Out-of-Hospital MACE (Death, QMI, NQMI, TLR, Emergent CABG)	2.0% (6)[0.7%, 4.3%]
MACE to 180 days (Death, QMI, NQMI, TLR, Emergent CABG)	5.7% (17)[3.4%, 9.0%]
MACE to 270 days (Death, QMI, NQMI, TLR, Emergent CABG)	10.1% (30) [6.9%,14.1%]
TLR rate at 180 days	3.4% (10) [1.6%,6.1%]
TLR rate at 270 days	7.0% (21) [4.4%, 10.6%}
TVR rate at 180 days	1.7% (5)[0.5%,3.9%]
TVR rate at 270 days	2.3% (7)[0.9%, 4.8%]
TVF rate at 180 days	6.7% (20) [4.1%, 10.2%]
TVF rate at 270 days	9.7% (29) [6.6%, 13.7%]
Bleeding Complications	2.3% (7)[0.9%,4.8%]
CVA	0.3% (1)[0.0%,1.9%]
Vascular Complications	3.4% (10)[1.6%,6.1%]
Stent Thrombosis	0.0% (0)[0.0%,1.2%]

MACE: Major Adverse Cardiac Event (includes death, MI, and emergent CABG or target lesion revascularization).

TLR free: No target lesion revascularization.
TVR free: No target vessel revascularization.
TVF free: No death, any MI or target vessel revascularization.
Binary restenosis: 50% or greater in-stent diameter stenosis at the follow-up angiogram.
Stent Thrombosis: Stent thrombosis was defined as total thrombotic stent occlusion documented by angiography.
In-hospital major clinical event: death, MI, emergent CABG, repeat target lesion revascularization, stent thrombosis, or stroke prior to discharge, as determined by the independent Clinical Events Committee.
Out-of-hospital major clinical event: death, MI, emergent CABG, repeat target lesion revascularization, stent thrombosis, or stroke after discharge, as determined by the independent Clinical Events Committee.
Vascular complications; may include pseudoaneurysm, arteriovenous fistula, peripheral ischemia/nerve injury or vascular event requiring transfusion or surgical repair.
Bleeding complications: transfusions due to blood loss resulting from the percutaneous revascularization procedure.
CVA: sudden onset of vertigo, numbness, dysphasia, weakenss, visual field defects, dysarthria or other focal neurological deficits due to vascular lesions of the brain, such as hemorrhage, embolism, thrombosis, or rupturing aneurysm, that persists greater than 24 hours.
Device success: Attainment of <30% in-stent residual stenosis using the randomized treatment strategy only.
Procedure success: <50% stenosis in-stent (or in-lesion if no in-stent measurement available) and freedom from in-hospital major adverse cardiac events (death, MI, emergent CABG, or repeat target lesion revascularization).
*Survival estimates by Kaplan-Meier method; Standard Error estimates by Greenwood formula

PREDICT Trial

Based on acceptable performance in de novo lesions and the similarities in design and manufacture of the Driver™ Coronary Stent System to the Medtronic S670™ and Medtronic S7 Coronary Stent Systems, the following study, which evaluated direct stenting using the Medtronic S670 Coronary Stent, also supports the suitability of direct stenting for delivery of the Medtronic Driver™ Coronary Stent System.

The PREDICT Trial was a prospective, multi-center study using the S670™ OTW Coronary System randomized to either direct stenting or standard predilatation deployment technique. The study was conducted at 37 North American clinical sites and included a total of four hundred (400) randomized patients and sixteen (16) roll-in patients with *de novo* native coronary artery lesions. A clinical events committee adjudicated all major clinical events and clinically driven TLR.

Primary Endpoint

The primary endpoint in the PREDICT Trial was Major Adverse Cardiac Event (MACE) rate defined as the composite of death, Q wave and non-Q wave myocardial infarction, emergent coronary artery bypass surgery, or target lesion revascularization (TLR) at 14 days.

Patients Studied

The 399 patients (65.7% male) treated ranged in age from 29 to 87 years with an average of 64 ± 11.6 (mean ± SD) years. All patients presented with angina or a positive functional study and were undergoing elective single *de novo* lesion treatment in a native coronary artery. Eligible patients had visually estimated stenosis ≤ 15 mm in length in a major coronary artery or major side branch ≥ 3.0 mm and ≤ 4.0 mm in diameter. One patient withdrew consent after randomization but before investigational treatment was attempted.

Methods

Patients in the PREDICT Trial were randomized to either direct stenting (without predilatation) or standard pre-dilatation by balloon angioplasty (1:1 balloon to artery ratio) after which a stent system(s) of the appropriate length and diameter was selected and deployed. The Medtronic AVE S670™ OTW stent delivery system could be repressurized up to 16 atm to further dilate the stent to assure complete apposition of the stent to the artery wall. If needed, further inflations were performed with a non-compliant balloon with a balloon-to-artery ratio of 1:1. Clinical follow-up was conducted up to 6 months.

The anticoagulation regimen administered to 97% (389/399) of the patients at discharge was 325 mg aspirin and either 500 mg ticlopidine or 300 mg clopidogrel. The follow-up

regimen administered to 83% (333/399) of the patients was 325 mg/day ASA for at least six month; ticlopidine 250 mg twice a day or clopidogrel 75 mg daily.

Clinical follow-up intervals for all treated PREDICT patients were 14 days, 30 days and 6 months. All patients underwent angiographic follow-up at 6 months for the PREDICT Trial. The study randomization was successful, as both treatment groups were demographically equivalent. All treated randomized patients were included in the intent-to-treat efficacy analysis. The principal effectiveness and safety for the PREDICT Trial for direct stenting versus predilatation are shown in the table below.

Conclusions

The success rate for the direct stenting arm was 92.0% (185/201). The sixteen patients who crossed over to the pre-dilatation arm were treated successfully. There were no statistically significant differences between the two arms with respect to Major Adverse Cardiac Events.

Principal Effectiveness and Safety Results PREDICT Trial
S670 PREDICT Patients Treated (N = 399)

Efficacy Measures	Direct Stenting (N=198 Patients, N=201 Lesions)	Pre-Dilatation (N=201 Patients, N=203 Lesions)	All Randomized* (N=399 Patients, N=404 Lesions)	Relative Risk [95% C.I.]	Difference [95% C.I.]	P-value
Primary Device Success	92.0% (185 / 201)	96.6% (196 / 203)	94.3% (381 / 404)	0.95 [0.91,1.00]	-4.5% [-9.0%,0.0%]	0.056
Secondary Device Success	99.5% (200 / 201)	99.0% (200 / 202)	99.3% (400 / 403)	1.00 [0.99,1.02]	0.5% [-1.2%,2.2%]	1.000
Procedure Success	93.9% (186 / 198)	92.5% (185 / 200)	93.2% (371 / 398)	1.02 [0.96,1.07]	1.4% [-3.5%,6.4%]	0.691
Post-Procedure In-Lesion Minimal Lumen Diameter (MLD, in mm)						
Mean±SD (N)	2.54±0.55 (199)	2.56±0.50 (199)	2.55±0.52 (398)	N/A	-0.02 [-0.12,0.09]	0.739
Range (min,max)	(1.34,4.29)	(1.37,4.01)	(1.34,4.29)			
Post-Procedure In-Lesion Percent Diameter Stenosis (% DS)						
Mean±SD (N)	18.9%±9.8% (199)	18.3%±11.1% (199)	18.6%±10.5% (398)	N/A	0.6% [-1.5%,2.6%]	0.585
Range (min,max)	(1.5%,55.6%)	(-27.7%,54.2%)	(-27.7%,55.6%)			
Post-Procedure In-Stent Minimal Lumen Diameter (MLD, in mm)						
Mean±SD (N)	2.92±0.43 (199)	2.98±0.42 (199)	2.95±0.43 (398)	N/A	-0.06 [-0.14,0.03]	0.185
Range (min,max)	(1.84,4.30)	(2.10,4.34)	(1.84,4.34)			
Post-Procedure In-Stent Percent Diameter Stenosis (% DS)						
Mean±SD (N)	5.9%±9.4% (199)	4.5%±9.3% (199)	5.2%±9.4% (398)	N/A	1.4% [-0.5%,3.2%]	0.150
Range (min,max)	(-24.1%,35.8%)	(-34.7%,27.0%)	(-34.7%,35.8%)			
In-Lesion Acute Gain (mm)						
Mean±SD (N)	1.60±0.60 (199)	1.66±0.58 (199)	1.63±0.59 (398)	N/A	-0.06 [-0.18,0.06]	0.302
Range (min,max)	(0.11,3.74)	(0.06,2.97)	(0.06,3.74)			
In-Stent Acute Gain (mm)						
Mean±SD (N)	1.98±0.53 (199)	2.08±0.52 (199)	2.03±0.53 (398)	N/A	-0.10 [-0.20,0.00]	0.056
Range (min,max)	(0.77,3.74)	(0.34,3.59)	(0.34,3.74)			
In-Lesion Binary Restenosis Rate	26.5% (43 / 162)	25.8% (42 / 163)	26.2% (85 / 325)	N/A	0.8% [-8.8%,10.3%]	0.900
In-Stent Binary Restenosis Rate	20.4% (33 / 162)	20.9% (34 / 163)	20.6% (67 / 325)	N/A	-0.5% [-9.3%,8.3%]	1.000
TLR-free to 180 days†	80.2%	82.6%	81.5%	0.97 [0.78,1.21]	-2.4% [-20.0%,15.3%]	0.846
TVR-free to 180 days†	79.3%	79.3%	79.3%	1.00 [0.80,1.26]	0.0% [-18.1%,18.1%]	0.643
TVF-free to 180 days†	72.9%	72.5%	72.7%	1.01 [0.77,1.32]	0.4% [-19.4%,20.1%]	0.677
MACE-free to 180 days†	73.8%	74.5%	74.1%	0.99 [0.76,1.29]	-0.7% [-20.2%,18.9%]	0.770
Safety Measures and Other Clinical Events						
In-Hospital MACE	5.6% (11 / 198)	7.0% (14 / 201)	6.3% (25 / 399)	0.80 [0.37,1.71]	-1.4% [-6.2%,3.3%]	0.681
Out-of-Hospital MACE to 14 days	0.5% (1 / 198)	0.5% (1 / 201)	0.5% (2 / 399)	1.02 [0.06,16.17]	0.0% [-1.4%,1.4%]	1.000
MACE to 14 days	6.1% (12 / 198)	7.5% (15 / 201)	6.8% (27 / 399)	0.81 [0.39,1.69]	-1.4% [-6.3%,3.5%]	0.691
Out-of-Hospital MACE to 180 days	13.1% (26 / 198)	13.9% (28 / 201)	13.5% (54 / 399)	0.94 [0.57,1.55]	-0.8% [-7.5%,5.9%]	0.884
MACE to 180 days	18.7% (37 / 198)	19.4% (39 / 201)	19.0% (76 / 399)	0.96 [0.64,1.44]	-0.7% [-8.4%,7.0%]	0.899
Abrupt Closure to 180 days	0.0% (0 / 198)	1.5% (3 / 201)	0.8% (3 / 399)	0.00 [—,—]	-1.5% [-3.2%,0.2%]	0.248
Subacute Closure to 180 days	0.0% (0 / 198)	0.5% (1 / 201)	0.3% (1 / 399)	0.00 [—,—]	-0.5% [-1.5%,0.5%]	1.000
Stent Thrombosis to 180 days	0.5% (1 / 198)	0.5% (1 / 201)	0.5% (2 / 399)	1.02 [0.06,16.17]	0.0% [-1.4%,1.4%]	1.000
CVA to 180 days	0.0% (0 / 198)	0.0% (0 / 201)	0.0% (0 / 399)	— [—,—]	0.0% [—,—]	N/A
Bleeding Complications to 180 days	1.5% (3 / 198)	1.0% (2 / 201)	1.3% (5 / 399)	1.52 [0.26,8.91]	0.5% [-1.7%,2.7%]	0.684
Vascular Complications to 180 days	7.1% (14 / 198)	4.0% (8 / 201)	5.5% (22 / 399)	1.78 [0.77,4.09]	3.1% [-1.4%,7.6%]	0.194

†. One patient withdrew consent after randomization but before the investigational treatment was attempted and was deregistered.

Primary Device Success = The attainment of a <50% residual in-stent (or in-lesion in the absence of in-stent) stenosis (by QCA) of the target site using the assigned treatment strategy alone, (i.e. only the Medtronic AVE S670™ stent without pre-dilatation if so randomized) during the index catheterization. If QCA was not available, the visual estimate of diameter stenosis was used. Post-dilatation with a high pressure or larger balloon was considered part of the treatment strategy for both arms, but tracked as to frequency. The need for pre-dilatation in patients randomized to direct stenting arm was considered a primary device failure and use of other brands of stents besides the Medtronic AVE S670™.

Secondary Device Success = The attainment of a <50% residual in-stent (or in-lesion in the absence of in-stent) stenosis (by QCA) of the target site using any strategy (including stent withdrawal, pre-dilatation or pre-treatment with another device, and a repeat attempt at stent implantation). If QCA was not available, the visual estimate of diameter stenosis was used. Post-dilatation with a high pressure or larger balloon was considered part of the treatment strategy for both arms, but tracked as to frequency.

Procedure Success = The attainment of a <50% in-stent (or in-lesion in the absence of in-stent) residual stenosis (by QCA) at the target site using any strategy and freedom from Major Adverse Cardiac Events prior to hospital discharge. If QCA was not available, the visual estimate of diameter stenosis was used.

In-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target lesion revascularization prior to discharge as determined by the independent Clinical Events Committee.

Out-of-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target lesion revascularization from hospital discharge through the 180-day contact, as determined by the independent Clinical Events Committee.

TLR-free = No target lesion revascularization.

TVR-free = No target vessel revascularization.
TVF-free = No death, MI, or target vessel revascularization.
Footnotes are continued on the following page.
MACE-free = No death, MI, emergent CABG, or target lesion revascularization.
Abrupt Closure = Occurrence of new severely reduced flow (TIMI grade 0 or 1) within the target vessel that persisted and required rescue by a non-assigned treatment strategy, or resulted in MI or death.
Subacute Closure = Abrupt closure that occurred after the index procedure was completed and within 30 days of the index procedure.
Stent Thrombosis = Angiographic thrombus or subacute closure within the stented vessel, or any death not attributed to a non-cardiac cause in the absence of documented angiographic stent patency within the first 30 days.
CVA = Acute neurological deficits recorded by the clinical sites that persisted >24 hours.
Bleeding Complications = Defined as transfusions of blood products due to blood loss from the percutaneous revascularization procedure.
Vascular Complications = Defined as hematoma >4 cm, false aneurysm, AV fistula, retroperitoneal bleed, peripheral ischemia/nerve injury, procedure related transfusion or vascular surgical repair.
Acute Gain = Acute gain was defined as the immediate dimensional change in minimal luminal diameter (in mm) that occurred as a result of the procedure, measured by quantitative coronary angiography based on data interpolated from two orthogonal views at baseline and after the final post dilatation.

X. CONCLUSIONS DRAWN FROM THE STUDIES

Pre-clinical Studies

The Medtronic Driver™ Stent Delivery System successfully passed all relevant biocompatibility testing conducted in accordance with ISO 10993: Biological Evaluation of Medical Devices. Furthermore, *in vivo* studies showed the radiopacity of the Driver stent to be equivalent to stainless steel controls; other characteristics such as deliverability and acute performance were rated fair to excellent. Histomorphometric analysis at 28, 90, and 180-days show the Driver™ Stent is statistically equivalent to the stainless steel control.

In Vitro Testing

The Medtronic Driver™ Stent Delivery System successfully passed all *in vitro* testing as required per the FDA guidance document, "Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices: PTCA Catheters, Atherectomy Catheters, Lasers, Intravascular Stents", May 1994.

Clinical Study

The 298-patient Medtronic Driver™ De Novo and Restenotic Registry successfully demonstrated the safety and effectiveness of the Driver™ Stent Delivery System in patients followed to 270 days. A comparison of the MACE rate at 180 days to the OPC of 15% demonstrated non-inferiority of the Driver™ Coronary Stent System to the OPC.

The 399-patient PREDICT trial performed direct stent in de novo lesions using the approved Medtronic S670™ stent. Due to the similarities in design and manufacture of the Medtronic S670™ and S7 stents, both of which are approved for direct stenting, the PREDICT trial supports direct stenting in de novo lesions for the Driver™ stent.

Conclusions Drawn from all Studies

The *in vitro* and *in vivo* non-clinical laboratory studies, together with the clinical investigation, provide valid scientific evidence and reasonable assurance that the

Medtronic Driver™ Stent System is safe and effective for its intended use in the treatment of patients presenting with symptomatic ischemic heart disease due to single *de novo* or restenotic lesions (no greater than 30 mm in length) in native coronary arteries with reference vessel diameters ranging from 3.0 mm to 4.0 mm.

XI. PANEL RECOMMENDATION

Pursuant to section 515 (c) (2) of the Federal Food, Drug and Cosmetic Act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory panel, for review and recommendation because the information in the PMA substantially duplicated information previously reviewed by this panel and raises no new issues of safety or effectiveness related to coronary stents.

XII. CDRH DECISION

The applicant's manufacturing facilities were inspected and found to be in compliance with the Quality System Regulation (21 CFR 820). FDA issued an approval order on October 1, 2003.

XIII. APPROVAL SPECIFICATIONS

Directions for use:
See the labeling.

Hazards to Health from Use of the Device:
See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Postapproval Requirements and Restrictions:
See approval order.